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09/413,110	10/06/1999	EVAN C. UNGER	UNGR-1580	1596

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EXAMINER	
SHARAREH, SHAHNAM J	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/413,110	UNGER, EVAN C.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *116-131,138-141,146-151,160,164-166,168-174 and 178-250* is/are pending in the application.

4a) Of the above claim(s) *185 -250* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *116-131, 138-141, 146-151, 160, 164-166, 168-170, 173-174, 178-184* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on November 10, 2005 has been entered. Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178-250 are pending.

2. Newly submitted claim 185-250 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the newly added claim are directed to different bioactive agents which were not originally elected as the species to be examined. In response to the election of species requirement filed on April 10, 2001, Applicant elected thrombolytic agents as the species of choice for the genus of bioactive agents (see Response to Election of Species Requirement filed on May 07, 2001). The Examination on the merits of claims have since been directed to such methods employing thrombolytic agents as the bioactive agents as the elected species. All other claims not directed to such species were then withdrawn from further prosecution. Since the claims directed to the use of such species are not allowable, restriction is proper between said the elected species and all other species of bioactive agents. (MPEP. 806.05(I)).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 185 -250 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 116-131, 138-141, 146-151, 160, 164-166, 168-170, 173-174, 178-184 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al US Patent 5,695,460 in view of Porter US Patent 5,648,098 for the reasons of record.

Claims 116 –120, 160, 164-166, 171-174, 178-184 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schlief US Patent 5,380,411 in view of Holmes et al (J. UROL. 144: 159-163, 1990) for the reasons of record.

Response to Arguments

4. Applicant's arguments filed November 10, 2005 have been fully considered but they are not persuasive.

5. Applicant argues that the instant methods are directed to cavitating or rupturing the vesicles at ultrasonic frequencies between about 750 kHz and 3 MHz and that there is nothining in the Siegel patent showing that an optimization of Siegel's frequencies are sought or desired. (see Arguments at page 18). Applicant then relying on *In re Brower*, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996) concludes that there would have been not motivation to modify the Siegel reference towards the instant claims. (see arguments at page 18-19).

6. As the initial matter, Applicant's reliance on *Brower* is misplaced. The factual scenario in *Brower,* by no means, resembles the case at bar. In *Brower* the Court reversed the Examiner because the rejection improperly relied on Applicant's disclosure and lacked any teachings of prior art providing a suggestion or motivation either to use

a specific reactant in a generic Chemical Reaction or to obtain a specific catalyst from a generic Chemical Reaction. Here, the teachings of the prior art not only teach the all method steps of the instant claims, but also the specific frequencies that can provide adequate thrombolytic activity.

7. Moreover, here, the question is whether a particular parameter in a process claim can be optimized by one of ordinary skill in the art to achieve better results. As a general rule articulated *In re Antoine*, any parameters that are clearly established in the art to affect the end-results desired are categorized as a result-effective parameter. *In re Antoine*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977), at 619-620

Here, the rejection only relies on optimization the ultrasound waves of the frequency described in Siegel to provide better cavitation and release of bioactive drugs at a site of interest. The rejection is not based on a general optimization of any or all other parameter that can vary the end clinical result, which is the release of the bioactive drugs. Examiner states that for purposes of enhancing drug release, various parameters can modify the end-clinical results. Such parameters include frequency of ultrasound waves, frequency of exposure, duration of ultrasound exposure, the type of ingredient forming the delivery systems, the type of gaseous precursors, the site of interest etc...

However, the only parameter that is described in the rejection for optimization is the frequency of ultrasound waves. Examiner adds that such ration is due to specific references of in the teaching of both Siegel and Porter. This reasoning is consistent to the anology used in *In re Antoine*, because Examiner does not argue that it would have

been obvious for one of ordinary skill in the art to try varying every parameter of the process in order to optimize the effectiveness of the therapy. Rather, those parameters that are clearly established in the art to affected the result.

8. As argued throughout the prosecution, Examiner states that Siegel does not discourage one of ordinary skill in the art to employ the frequencies instantly claimed. Siegel at col 5, lines 29-31 states that it has been found that when ultrasound is applied at a lower, rather than a higher frequency, the effectiveness of the method is markedly enhanced. The recitation of "higher frequencies" as used by Siegel does not teach against the instantly claimed ranges. In fact such recitation is relative and viewed to be open to optimization. One of ordinary skill in the art would have most likely performed further experimentation to determine what is the highest range of ultrasound frequencies capable of producing the same results described in Siegel.

9. Finally, the element of motivation in an obviousness rejection considers the understanding of one of ordinary skill in the art and not merely the teachings of one publication. Examiner concludes that a person of one ordinary skill reading the Siegel's reference would have been in possession of many teachings published prior to Siegel describing the use of ultrasound energy and various ultrasound emitting apparatus for enhancing local drug delivery. One of such publications include Porter describing various ranges of ultrasound frequencies for drug delivery, as well as, Zohar US Patent 5,076,208 published in December of 1991, describing the use of ultrasound for administering drugs in an aquatic animals using a frequency of about 1MHz. Thus, the ordinary skill in the art would not have been discouraged from optimizing the path set

out by Siegel, or would have taken a direction divergent from the path that was taken by the applicant, and modifying the ultrasound frequencies or the rate of infusion would have been achieved by routine experimentation.

10. Furthermore, Porter shows that the state of art does not discourage the use of instantly claimed ultrasound frequencies for drug delivery. (see col 4, lines 48-50). Porter specifically provides for the use of the claimed frequencies. Thus, their combined teachings would have rendered the instant claims obvious, because one of ordinary skill in the art would have had a reasonable expectation to succeed in optimizing the rate of administration or ultrasound frequencies to improve availability of contrast agents and the end clinical outcome.

11. With respect to the rejection of claims over Schlief and Holmes, Applicant states that there is nothing in Holmes that one of skill in the art can learn from for the purposes of the present application. (*see* Arguments at page 20). Applicant adds that the expression of "high energy shock waves" is relative and would be speculation to guess what such frequencies were meant. *Id.*

In response, Examiner states that as discussed above, the rejection is based on whether one of ordinary skill in the art can optimize a result-effective parameter that is described in the prior art. Here, Holmes describes such parameter to be "high energy shock waves." Applicant has not provided any evidence that such waves cannot be within the ranges instantly claimed, or is not optimizable to such degree that falls within the scope of the instantly claimed ranges. Accordingly, the arguments are not found persuasive.

Conclusion

12. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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SUPERVISORY PATENT EXAMINER